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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,723	01/17/2001	Yasuo Koishihara	53466/295	4861

22428 7590 02/04/2008
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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
02/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/760,723	KOISHIHARA, YASUO	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,20 and 23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,20 and 23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 10/31/07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks filed 10/31/07 have been entered.

2. Claims 13, 20, 23, 24, and newly added Claims 25-32 are pending and being acted upon.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 13, 20, 23, 24, and newly added Claims 25-32 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,298,420 (1994) in view of Goto, T., et al. (1994, IDS) for the reasons of record.

As set forth previously, The '420 patent teaches a method of inhibiting B lymphocyte activation (by killing the lymphocyte) for the treatment of an autoimmune disease or a B cell cancer comprising administering a monoclonal antibody which binds B cells (see particularly column 1, lines 27-39 and column 6, lines 45-57).

The reference teaching differs from the claimed invention only in that it does not teach the use of the chimeric, humanized monoclonal antibody HM1.24 which binds SEQ ID NO:1.

Goto, T., et al. teaches the use of the chimeric, humanized monoclonal antibody HM1.24 which binds SEQ ID NO:1 on terminally differentiated B cells for the treatment of multiple myeloma (see particularly page 1922, column 2, paragraph 1 and page 1929, column 1 paragraph 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method of inhibiting B lymphocyte activation (by killing the lymphocyte) for the treatment of an autoimmune disease,

comprising administering a monoclonal antibody, as taught by the '343 patent, employing the humanized monoclonal antibody HM1.24 which binds SEQ ID NO:1, as taught by Goto, T., et al. as the specific monoclonal antibody. One of ordinary skill in the art at the time the invention was made would have been motivated to use the HM1.24 because said antibody was known to selectively bind terminally differentiated B cells, as taught by Goto, T., et al., and would thus, be an obvious choice for the elimination of said cells and the treatment of any disease (such as a B cell-mediated autoimmune disease) which said cells mediate. Note that the substitution of equivalents, in this instance different B cell-binding antibodies, is considered to be obvious.

Applicant's arguments, filed 6/27/07, have been fully considered but they are not persuasive. Applicant alleges that the presently claimed antibodies provide unexpected advantages.

The instant claims are drawn to a method of inhibiting activated lymphocytes or treating a disease associated with lymphocyte activation employing an antibody. The claims are not drawn to the well-known antibody itself. Regardless, allegations regarding unexpected results or advantages require significant substantiation which has not been provided.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25-32 (replacing now amended Claims 13 and 15-24) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the antibody employed in the claims could bind T lymphocytes as is required by the claimed method.

As set forth previously, a further review of Goto et al. shows that the reference teaches that the anti-HM1.24 antibody is B cell specific. Table 1 teaches that the antibody does not bind T cells. Thus, the teachings of Goto et al. directly contradict the findings of the instant disclosure. The most scientifically reasonable conclusion would be that the antibody binds some T cells (i.e., the T cells of the specification), but not others (i.e., the T cells of

Goto et al.). Clearly then, an unpredictability has been established, at least as the claimed invention encompasses a method that requires the binding of the amino acid sequence of SEQ ID NO:1 and the binding of T cells.

The specification makes clear that the HM1.24 antibody of the claims is the antibody of Goto et al. (1994) as Goto et al. is cited as the source. It must have been clear to the Inventors that their findings contradicted the findings of the actual producers of the antibody used, and that the issue would arise during examination. Yet the Inventors chose not to address this critical difference in the findings. It remains then that the unpredictability cited in the rejection has been established and that sufficient evidence to overcome said unpredictability as not been made of record.

Applicant's arguments, filed 10/31/07 have been fully considered but they are not persuasive. Applicant argues that the amended claims render the rejection moot.

Applicant is correct regarding the amended claims. Newly presented Claims 25-32, however, encompass the inhibiting of T lymphocytes (as well as B lymphocytes), thus, the rejection remains for the reasons set forth in the body of the rejection.

7. Claims 13, 20, 23, 24, and newly added Claims 25-32 stand/are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter written description rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a method of inhibiting the activity of activated lymphocytes…,

B) a method of treating a disease associated with lymphocyte activation…,

C) a method employing an antibody wherein the antibody has an L chain V region of SEQ ID NO:2, and an H chain V region selected from the group consisting of SEQ ID NO:3 and SEQ ID NO:4.

Applicant cites page 21 and Example 2 (pages 28-30) in support of the claimed method.

None of the cites teach the claimed method of inhibiting activity of activated lymphocytes or a method of treatment. At

page 25 the specification merely discloses that the inhibitors of lymphocyte activation may be administered. Further, nowhere in the specification is the antibody of C) above disclosed.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 25-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, there cannot be an antibody with an H chain V region of SEQ ID NO:4 because SEQ ID NO:4 encodes a polynucleotide.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571)272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, Ph.D. can be reached on (571) 272-0878.

12. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

1/31/08

G.R. Ewoldt, Ph.D.
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Technology Center 1600